

Appln. No. 09/660,328
Amd. dated November 17, 2003
Reply to Office Action of September 16, 2003

Amendments to the Claims

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

Claims 1-51 (Cancelled).

52 (Currently amended). [[A]] The method of claim 113, which is for diagnosing prostate cancer, comprising:

a) obtaining cells wherein the cells in step (a) are obtained from a body fluid in an individual suspected to have prostate cancer; and

b) determining the synchrony in replication timing between alleles of one or more DNA loci in said cells, wherein a determination of asynchrony between alleles of one or more DNA loci, which replicate synchronously in normal diploid cells, or a determination of synchrony between alleles of one or more DNA loci, which replicate asynchronously in normal diploid cells, provides positive predictability of prostate cancer in the individual.

53 (Previously presented). The method of claim 52, wherein the cells are subjected to a growth stimulus before step (b).

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54 (Previously presented). The method of claim 52,
wherein the cells are subjected to chromatin and/or DNA modifiers
before step (b).

55 (Previously presented). The method of claim 54,
wherein the cells are subjected to chromatin and/or DNA modifiers
selected from the group consisting of 5-azacytidine, Trichostatin
A, Sodium Butirate, and N-nitroso-n-methylurea.

56 (Previously presented). The method of claim 52,
wherein the body fluid is selected from the group consisting of
blood, amniotic fluid, urine, and saliva.

57 (Previously presented). The method of claim 56,
further including the step of isolating cells from bodily fluids.

58 (Previously presented). The method of claim 56,
wherein the blood is peripheral blood.

59 (Previously presented). The method of claim 58,
further including the step of isolating peripheral blood cells.

60 (Previously presented). The method of claim 52,
wherein the cells are lymphocytes.

61 (Previously presented). The method of claim 52,
wherein the locus or loci are non-coding DNA regions.

62 (Previously presented). The method of claim 52,
wherein the locus or loci are selected from satellite DNA
arrays.

63 (Previously presented). The method of claim 52,
wherein the locus or loci are centromere-associated.

64 (Previously presented). The method of claim 52,
wherein the locus or loci are tumor-associated genes.

65 (Previously presented). The method of claim 52,
wherein the locus or loci are selected from the group consisting
of oncogenes, tumor suppressor genes, and transcription factors.

66 (Previously presented). The method of claim 52,
wherein the locus or loci replicate synchronously in normal
diploid cells.

67 (Previously presented). The method of claim 66,
wherein the locus or loci are expressed biallelically.

68 (Previously presented). The method of claim 66,
wherein the locus or loci are selected from the group consisting

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of HER2, CMYC, TP53, RB1, D21S55, D15S10, D22S75 and DSTS WI-941 and alpha, II and III satellites for all chromosomes.

69 (Previously presented). The method of claim 52, wherein the locus or loci replicate asynchronously in normal diploid cells.

70 (Previously presented). The method of claim 69, wherein the locus or loci are expressed monoallelically.

71 (Previously presented). The method of claim 70, wherein the locus or loci are selected from the group consisting of GABRB3 and SNRPN.

72 (Previously presented). The method of claim 70, wherein the locus or loci are selected from imprinted loci, loci on the X-chromosome in female individuals, and loci subjected to allelic exclusion.

73 (Previously presented). The method of claim 72, wherein the imprinted locus is the Prader-Willi locus.

74 (Previously presented). The method of claim 52, wherein the determination of asynchrony is a change in synchrony

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of replication timing of between about 3% to about 55% relative to replication timing in normal individuals.

75(Previously presented). The method of claim 74, wherein the change in synchrony is an increase in asynchrony of between about 15% to about 35%.

76(Previously presented). The method of claim 74, wherein the change in synchrony is a decrease in asynchrony of about 10% to about 20%.

77(Previously presented). The method of claim 52, wherein synchrony of replication timing is determined by fluorescence *in situ* hybridization.

78(Currently amended). [[A]] The method of claim 113, which is for diagnosing breast cancer, comprising:

a) obtaining cells wherein the cells in step (a) are obtained from a body fluid in an individual suspected to have breast cancer; and

b) determining the synchrony between alleles of one or more DNA loci in said cells, wherein a determination of asynchrony between alleles of one or more DNA loci, which replicate synchronously in normal diploid cells, or a

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~~determination of synchrony between alleles of one or more DNA loci, which replicate asynchronously in normal diploid cells, provides positive predictability of breast cancer in the individual.~~

79 (Previously presented). The method of claim 78, wherein the cells are subjected to a growth stimulus before step (b).

80 (Previously presented). The method of claim 78, wherein the cells are subjected to chromatin and/or DNA modifiers before step (b).

81 (Previously presented). The method of claim 80, wherein the cells are subjected to chromatin and/or DNA modifiers selected from the group consisting of 5-azacytidine, Trichostatin A, Sodium Butirate, and N-nitroso-n-methylurea.

82 (Previously presented). The method of claim 78, wherein the body fluid is selected from the group consisting of blood, amniotic fluid, urine, and saliva.

83 (Previously presented). The method of claim 82, further including the step of isolating cells from bodily fluids.

84 (Previously presented). A method of claim 82,
wherein the blood is peripheral blood.

85 (Previously presented). The method of claim 84,
further including the step of isolating peripheral blood cells.

86 (Previously presented). The method of claim 78,
wherein the cells are lymphocytes.

87 (Previously presented). The method of claim 78,
wherein the locus or loci are non-coding DNA regions.

88 (Previously presented). The method of claim 78,
wherein the locus or loci are selected from satellited DNA
arrays.

89 (Previously presented). The method of claim 78,
wherein the locus or loci are centromere-associated.

90 (Previously presented). The method of claim 78,
wherein the locus or loci are tumor-associated genes.

91 (Previously presented). The method of claim 78,
wherein the locus or loci are selected from the group consisting
of oncogenes, tumor suppressor genes, and transcription factors.

92 (Previously presented). The method of claim 78, wherein the locus or loci replicate synchronously in normal diploid cells.

93 (Previously presented). The method of claim 92, wherein the locus or loci are expressed biallelically.

94 (Previously presented). The method of claim 92, wherein the locus or loci are selected from the group consisting of HER2, CMYC, TP53, RB1, D21S55, D15S10, D22S75 and DSTS WI-941 and alpha, II and III satellites for all chromosomes.

95 (Previously presented). The method of claim 78, wherein the locus or loci replicate asynchronously in normal diploid cells.

96 (Previously presented). The method of claim 95, wherein the locus or loci are expressed monoallelically.

97 (Previously presented). The method of claim 96, wherein the locus or loci are selected from the group consisting of GABRB3 and SNRPN.

98 (Previously presented). The method of claim 96, wherein the locus or loci are selected from imprinted loci, loci

on the X-chromosome in female individuals, and loci subjected to allelic exclusion.

99(Previously presented). The method of claim 98,
wherein the imprinted locus is the Prader-Willi locus.

100(Previously presented). The method of claim 78,
wherein the determination of asynchrony is a change in synchrony of replication timing of between about 3% to about 55% relative to replication timing in normal individuals.

101(Previously presented). The method of claim 100,
wherein the change in synchrony is an increase in asynchrony of between about 15% to about 35%.

102(Previously presented). The method of claim 100,
wherein the change in synchrony is a decrease in asynchrony of about 10% to about 20%.

103(Previously presented). The method of claim 78,
wherein synchrony of replication timing is determined by fluorescence *in situ* hybridization.

Claims 104-112 (Cancelled).

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113 (New). A method for diagnosing prostate or breast cancer, comprising:

- a) obtaining cells from a body fluid in an individual suspected to have prostate or breast cancer; and
- b) determining the synchrony in replication timing between alleles of one or more DNA loci in said cells, wherein a determination of asynchrony between alleles of one or more DNA loci, which replicate synchronously in normal diploid cells, or a determination of synchrony between alleles of one or more DNA loci, which replicate asynchronously in normal diploid cells, provides positive predictability of prostate or breast cancer in the individual.